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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	James E. Brehove
Serial No.:	10/077,521
Filed:	February 15, 2002
For:	**TOPICAL APPLICATION FOR TREATING TOENAIL FUNGUS**
Matter No.:	0045-1

Morristown, N.J. 07960
December 24, 2002

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

PETITION TO MAKE SPECIAL FOR NEW APPLICATION UNDER M.P.E.P. § 708.02 (VIII)

Applicant hereby petitions to make special this new application. The application has not yet been examined by the United States Patent and Trademark Office (the "Office").

Applicant submits that all of the claims in this case are directed to a single invention. If the Office determines that all claims presented are not obviously directed to a single invention, then applicant will make an election, without traverse, as a prerequisite to the grant of special status.

A pre-examination search of the subject matter encompassed by the above-identified application has been made by a professional searcher. The pre-examination search was conducted in the United States Patent and Trademark Office. The field of search covered Class 424, subclasses 61, 404 and 405 and class 514, subclass 64. Copies of the references developed by the pre-examination search are submitted with this petition. A statement pertaining to the pre-examination search listing the references deemed most closely related to the subject matter encompassed by the claims is submitted herewith.

Applicant also submits herewith a detailed discussion of the references, which discussion particularly points out how the claimed subject matter is distinguishable over the references.

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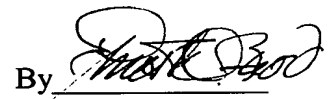
Enclosed herewith is a check in the amount of $130, to cover the fee for this Petition. In the event that any additional fee is deemed to be required by 37 C.F.R. 1.17(i), it is requested that applicants be contacted at (973) 644-0008 and provided an opportunity to effect payment thereof.

A duplicate of this petition is attached.

Respectfully submitted,
James E. Brehove

By 
Ernest D. Buff
(His Attorney)
Reg. No. 25,833
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0045-1-PMS-P1

OIPE JC106 DEC 30 2002 PATENT & TRADEMARK OFFICE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: James E. Brehove
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Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

STATEMENT PERTAINING TO PRE-EXAMINATION SEARCH IN ACCORDANCE WITH MPEP § 708.02(VIII)

In accordance with MPEP § 708.02 (VIII), applicants, by and through their attorney, hereby submit that a pre-examination search was made for the above-identified application. The search was conducted by applicants' agents at the United States Patent and Trademark Office. The field of search covered covered Class 424, subclasses 61, 404 and 405 and class 514, subclasses subclass 64. Examiner Therman Page in Class 424 was consulted in confirming the field of search.

The search identified the following references:

UNITED STATES PATENTS

U.S. Patent Number	Inventors(s)
2,741,548	Darling et al.
3,009,799	Dykstra
3,189,637	Bengelsdorf et al
3,510,554	Balsiger et al.
3,877,890	Maisey et al.
4,718,919	DeLue

UNITED STATES PATENTS (CTD.)

U.S. Patent Number	Inventors(s)
4,742,044	Boden
5,346,692	Wohlrab, et al.
5,391,367	DeVincentis et al.
5,464,610	Hayes, Jr. et al.
5,487,776	Nimini
5,696,105	Hackler
5,760,052	Peacock
5,840,283	Sorenson et al.
5,866,105	Richter, et al.
5,874,476	Hsu et al.
5,916,545	Burnett et al.
5,972,317	Sorenson et al.
6,022,549	Dyer

NON-PATENT REFERENCES

Title	Author
"Boron Compounds, Safety Profile"	Lewis Sr., R.J.
"Recherches Parmacologique sur les Dérivés Organiquyes du Bore (Etude du méthyl$_5$, propyl$_5$, p.tolyl$_2$, dioxaborinane)"	Caujolle, F. et al.
Material Safety Data Sheet BIOBOR JF®	

Each of the foregoing references has been identified and discussed in the Detailed Discussion of the References Submitted in Compliance with MPEP § 708.02(VIII).

Respectfully submitted,
James E Brehove

By [redacted]
Ernest D. Buff
(His Attorney)
Reg. No. 25,833
(973) 644-0008

0045-1-PMSS1

E.I.P.E. JC106
DEC 30 2002
PATENT & TRADEMARK OFFICE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	James E. Brehove
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Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

DETAILED DISCUSSION OF THE REFERENCES SUBMITTED WITH THE INFORMATION DISCLOSURE STATEMENT IN COMPLIANCE WITH MPEP § 708.02 (VIII)

In accordance with MPEP § 708.02(VIII), applicants hereby submit a detailed discussion of references applicable to the above-identified application. Each of these references was listed in the Information Disclosure Statement filed with the United States Patent and Trademark Office on May 25, 2002 in connection with the above-identified application.

A. U.S. Patent No. 2,741,548 to Darling, et al.

U.S. Patent 2,741,548 to Darling, et al. (hereinafter the '548 patent) discloses admixing organo-boron additives with leaded motor fuel to ameliorate the buildup of lead deposits. The '548 patent describes two genera comprising 2,2' -(alkyldioxy) bis- (alkyl-1, 3,2-dioxaborinane) and 2,2'-oxybis(alkyl-1, 3,2-dioxaborinane) derivatives. 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) of the present invention is a member of the first genus but is not expressly disclosed. 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) is a member of the second genus and is expressly disclosed.

Unlike the present invention, the '548 patent is limited to a leaded fuel composition. 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) is not expressly disclosed in the '548 patent. 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) is disclosed by the '548 patent; but for the purpose of preventing lead buildup. In contrast, applicant's claims are directed to use of the compound for the topical treatment of toenail fungus. Accordingly it is submitted that the '548 patent presents no obstacle to patenting of either 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or the combination of 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) and 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) for the treatment of onychomycosis.

B. U.S. Patent No. 3,009,799 to Dykstra

U.S. Patent 3,009,799 to Dykstra (hereinafter the '799 patent) discloses, "... new jet fuel compositions which are characterized by a high degree of thermal stability." The '799 patent describes a genus and several species of jet fuel additives comprising 2,2' - (alkyldioxy) bis-(alkyl-1, 3 , 2-dioxaborinane) derivatives, termed "biborates" by the patentee. 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) of the present invention is a member of this genus but is not expressly disclosed in the patent. 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) of the present invention is not a member of this genus.

The '799 patent discloses a genus of compounds including 2,2' -(alkyldioxy) bis-(alkyl-1, 3 , 2-dioxaborinane) derivatives to improve the thermal stability of jet fuel compositions. 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) is not expressly disclosed in the patent, and 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) is not a member of the genus

called for by the patent claims. For the above reasons it is submitted that the applicants' claimed topical treatment of toenail fungus patentably differentiates the '799 patent.

C. U.S. Patent No. 3,189,637 to Bengelsdorf, et al.

U.S. Patent 3,189,637 to Bengelsdorf, et al. (hereinafter the '637 patent) discloses cycloalkenyl glycol boric acid esters including 2,2' -(alkyldioxy) bis-(alkyl-1, 3, 2-dioxaborinane) derivatives. These compounds are said to have utility in a variety of applications including as fuel additives, corrosion inhibitors, anti-gumming agents herbicides, fungicides, bacteriostatic agents and in the production of resins, adhesives and coating compositions. The'637 patent lists two groups of reactants that may be combined to form the products it discloses. 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane)and 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) of the present invention are not expressly disclosed by the '637 patent. Moreover, neither 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) nor 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) may be derived from the reactants listed in the '637 patent. In addition, application of the cycloalkenyl glycol boric acid esters for treatment of onychomycosis, as called for by applicant's claims, is not disclosed. These distinctions are submitted to provide ample basis upon which patentability of applicants' claimed topical treatment of toenail fungus can be predicated.

D. U. S. Patent No. 3,510,554 to Balsiger et al.

U. S. Patent 3,510,554 to Balsiger et al., (hereinafter the '554 patent), discloses compositions and methods for hardening fingernails and toenails. The composition comprises tannic acid, distilled hamamelis water, chamomile extract, cognac and ethyl alcohol. A further composition comprises tannic acid, citric acid, distilled hamamelis water, spirits

of camphor, spirits of lavender, ethyl alcohol, tincture of garlic, chamomile extract, cognac, boric acid solution, bergamot oil and lavender oil.

The '554 patent does not disclose a composition including one species from the group consisting of 2,2' –(alkyldioxy) bis-(alkyl-1,3,2-dioxyborinane) and 2,2'-oxybis(alkyl-1,3,2-dioxaborinane) as defined by claim 1 of the present invention. More, specifically, the '544 patent does not disclose a composition including 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) as defined by present claim 2. In addition, the '544 patent does not disclose a topical treatment for toenail fungus, as called for by applicant's claims. These structural and functional distinctions patentably differentiate the topical treatment for toenail fungus claimed herein from the '554 patent disclosure.

E. U. S. Patent No. 3,877,890 to Maisey et al.

U. S. Patent 3,877,890 to Maisey et al. (hereinafter the "'890 patent"), discloses biocide compositions for controlling and preventing the growth of microorganisms in jet fuel. The organo-boron compounds of the '890 patent do not include the dioxaborinane genus of the present topical application nor 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane). Application of the biocides contained by the '890 patent compositions for the topical treatment of toenail fungus is not disclosed. For the above reasons it is submitted that the applicants' claimed composition and treatment method patentably define over the '890 patent disclosure.

F. U.S. Patent No. 4,718,919 to DeLue, et al.

U.S. Patent 4,718,919 to DeLue, et al. (hereinafter the '919 patent) discloses an anti-icing and biocidal and fungicidal fuel additive that includes, in combination, 2,2' -

(1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) together with an ethylene glycol monoalkylether. The species 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) are a subcombination of the combination disclosed in the '919 patent. Although the subcombination 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) has been broadly recited in the combination of the '919 patent, it has separate utility. Claims directed to the subcombination are, in such instances, patentably distinct when they recite specific characteristics not set forth in the combination claim [M.P.E.P. 806.05(c)I]. In this case, the formulation for the topical treatment of toenail fungus affords specific, advantageous characteristics, including safety, effectiveness and freedom from toxicity. These characteristics not disclosed or suggested by the '919 patent. Accordingly, claims drawn to a formulation consisting of 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) for the purpose of treating onychomycosis patentably distinguish the '919 patent disclosure.

Furthermore, claims drawn to a formulation having as its purpose the topical treatment of toenail fungus, and comprising 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) in combination with one of a skin permeable carrier solvent, a lacquer, a gel, a cream, or a proteolytic enzyme, would be novel over earlier disclosures teaching use of 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) as fuel additives. The presence of significant performance advantages, such as unexpected effectiveness and safety, as well as secondary considerations, including long-felt need, provide ample basis upon which to

predicate patentability of applicant's claims over the '919 patent. For the above reasons it is submitted that the composition and method defined by present claims 1 to 15 patentably distinguishes the '919 patent.

G. U.S. Patent 4,742,044 to Boden

U.S. Patent 4,742,044 to Boden (hereinafter the '044 patent) discloses 1,3,2 - dioxaborinane derivatives useful in augmenting or enhancing the aroma of perfume compositions and perfumed articles. 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) of the subject topical application are not expressly disclosed by the '044 patent. In addition, there is no suggestion that any of the patented compounds can be advantageously used for the treatment of onychomycosis. Based on these compositional and procedural distinctions, the invention defined by present claims 1-15 is patentably distinct from the disclosure of the '044 patent. These differences are submitted to provide the basis for predicating patentability of the topical treatment of toenail fungus claimed herein over the '044 patent teaching.

H. U. S. Patent No. 5,346,692 to Wohlrab et al.

U.S. Patent 5,346,692 to Wohlrab et al. (hereinafter the '692 patent) discloses a nail lacquer for treatment of onychomycosis. The composition for the treatment of toenail fungus comprises a polymeric film forming agent, at least one antimycotically active substance, urea and a solvent. The antimycotically active substances include clotrimazole, bifonazole, butaconazole, chlordantoin, chlormidazole, cloconazole, enilconazole, fenticonazole, isoconazole, ketoconazole, omoconazole, oxiconazole nitrate, and sulconazole. The antimycotically active substance and the urea are liberated from the lacquer when the lacquer is applied to the nail.

The '692 patent does not disclose a composition including one species from the group consisting of 2,2' –(alkyldioxy) bis-(alkyl-1,3,2-dioxyborinane) and 2,2'-oxybis(alkyl-1,3,2-dioxaborinane) as defined by claim 1 of the instant application. In addition, the '692 patent does not disclose a composition including 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) as defined by present claim 2. For the above reasons it is submitted that the applicants' claimed composition and treatment of toenail fungus patentably defines over the '692 patent disclosure.

I. U. S. Patent No. 5,391,367 to DeVincentis et al.

U.S. Patent 5,391,367 to Hara et al., (hereinafter the "'367 patent"), discloses a antifungal nail solution. The solution comprises tioconazole, water, alcohol, a water-soluble gel-forming agent and propylene glycol dipelargonate as a plasticizer. The plasticizer creates a reservoir for the antifungal compound, tioconazole, on the nail from which tioconazole continuously penetrates the nail.

The '367 patent does not disclose a composition including one species from the group consisting of 2,2' –(alkyldioxy) bis-(alkyl-1,3,2-dioxyborinane) and 2,2'-oxybis(alkyl-1,3,2-dioxaborinane) as defined by claim 1 of the present invention. Moreover, the '367 patent does not disclose a composition including 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) as defined by the present claim 2. For these reasons, the composition and method for the topical treatment of toenail fungus recited by present claims 1 to 15 is submitted to be patentable over the '367 patent.

J. U. S. Patent No. 5,464,610 to Hayes, Jr. et al.

U.S. Patent No. 5,464,610 to Hayes, Jr. et al., (hereinafter the '610 patent), discloses a method for treating onychomycosis without drilling a hole in the nail plate or without

daily scraping of the nail. The method comprises topically administering to the nail a medicated device including salicyclic acid, or a salt ester of salicylic acid, in a plaster preparation attached to a carrier. The carrier can be selected from a wide range of materials, especially those which can promote occlusion and hydration of the nail, such as a resin-impregnated woven cloth, flexible polyvinyl chloride film or a flexible polyester film.

The '610 patent does not disclose a method for the treatment of onychomycosis using one species from the group consisting of 2,2' –(alkyldioxy) bis-(alkyl-1,3,2-dioxyborinane) and 2,2'-oxybis(alkyl-1,3,2-dioxaborinane) as defined by claim 1 of the present invention. In addition, the '610 patent does not disclose a method including the use of 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) as defined by the present claim 2. The '610 patent neither teaches nor suggests the novel features of claims 1 to 15, namely a composition and method for the treatment of toenail fungus including an organo-boron compound. These features provide basis for predicating patentability of the topical treatment for onychomycosis claimed herein over the disclosure of the '610 patent.

K. U.S. Patent No. 5,487,776 to Nimini

U.S. Patent 5,487,776 to Nimini (hereinafter the '776 patent) discloses an anti-fungal nail lacquer and a method to use the lacquer on toenails or fingernails. The anti-fungal nail lacquer comprises an organic film former, a suspending agent and griseofulvin. The film forming compounds are in solution in a solvent system of one or more biocompatible organic solvents. The solvent systems may include lower alkyl alcohols such as ethyl, butyl and isopropyl alcohols, aromatic solvents such as benzyl alcohol, and butyl, ethyl, and amyl acetate. A relatively hard water permeable film remains after evaporation of the solvent. The film-forming compounds include

polymers and copolymers of vinyl acetate, polymers and copolymers of acrylic or methacrylic acid, polyvinylacytel and polyvinylbutyrals.

The '776 patent does not disclose a composition including one species from the group consisting of 2,2' –(alkyldioxy) bis-(alkyl-1,3,2-dioxyborinane) and 2,2'-oxybis(alkyl-1,3,2-dioxaborinane) as defined by claim 1 of the present invention. In addition, the '766 patent does not disclose a composition including 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) as defined by the present claim 2. Indeed, there is no disclosure in the '776 patent concerning a composition and method for the treatment of toenail fungus that includes an organo-boron compound. . For the above reasons it is submitted that the applicants' claimed composition and method patentably define over the '776 patent disclosure

L. U.S. Patent No. 5,696,105 to Hackler

U.S. Patent 5,696,105 to Hackler (hereinafter the '105 patent) discloses a method for treating onychomycosis with an anti-fungal nail composition. The composition consists essentially of 3,20 –dioxo-1,4 pregnadiene. The 3,20-dioxo-1, 4-pregnadiene is mometasone furoate in a pharmaceutically acceptable vehicle. Most preferably, the composition utilized in the treatment of onychomycosis is Elocon.RTM. mometasone furoate cream 1.0% topical composition that is sold by Schering Plough for Kenilworth, N.J. The pharmaceutically acceptable vehicle may comprise a hexylene glycol-containing cream or hydro-alcoholic lotion.

The '105 patent does not disclose a method and composition including one species from the group consisting of 2,2' –(alkyldioxy) bis-(alkyl-1,3,2-dioxyborinane) and 2,2'-oxybis(alkyl-1,3,2-dioxaborinane) as defined by claim 1 of the present invention. More generally, there is no disclosure in the '105 patent of a composition and method for the treatment of toenail fungus including an organo-boron compound. For these reasons, the composition and method for

the topical treatment of toenail fungus recited by present claims 1 to 15 is submitted to be patentable over the '105 patent.

M. U.S. Patent No. 5,760,052 to Peacock

U.S. Patent 5,760,052 to Peacock (hereinafter the '052 patent) discloses a composition for use as a fungistat and for the treatment of fungal infections. The composition comprises acriflavine and genetian violet.

The '052 patent does not disclose a composition including one species from the group consisting of 2,2' –(alkyldioxy) bis-(alkyl-1,3,2-dioxyborinane) and 2,2'-oxybis(alkyl-1,3,2-dioxaborinane) as defined by claim 1 of the instant application. Indeed, the composition disclosed by the '052 patent does not suggest a composition and method for the treatment of toenail fungus including an organo-boron compound. For the above reason it is submitted that the applicants' claimed composition patentably defines over the '052 patent disclosure.

N. U.S. Patent No. 5,840,283 to Sorenson et al.

U.S. Patent 5,840,283 to Sorenson et al. (hereinafter the '283 patent) discloses a nail-permeable composition for the treatment of a specific disease. Specifically, the nail-permeable compostion is particularly useful for treating onychomycosis of the fingernail or toenail. The nail-permeable composition comprises a proteolytic enzyme and a medicament. The medicament is selected from the group consisting of ciclopirox olamine, miconazole, itraconazole, clotrimazole, bifonazole, terbinafine, amorolfin, griseofulvin, econazole, and tolnaftate. The proteolytic enzyme is capable of temporarily modifying the cellular structure of the nail in a manner to permit permeation of medication through the nail without permanently harming the structural integrity of the nail. The proteolytic enzyme preferably may be selected from the group comprising papain, bromelain, chymotrypsin, trypsin.

The '283 patent does not disclose a composition including one species from the group consisting of 2,2' –(alkyldioxy) bis-(alkyl-1,3,2-dioxyborinane) and 2,2'-oxybis(alkyl-1,3,2-dioxaborinane) as defined by claim 1 of the present invention. In addition, the '283 patent does not disclose a composition including 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) or 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) as defined by the present claim 2. For these reasons, the composition and method for the topical treatment of toenail fungus recited by present claims 1 to 15 is submitted to be patentable over the '283 patent.

O. U.S. Patent No. 5,866,105 to Richter, et al.

U.S. Patent 5,866,105 to Richter et al. (hereinafter the '105 patent) discloses a composition and method for the treatment of onychomycosis. The active compound belongs to the class of allylamine anti-mycotics. It is known in the art under its generic name as terbinafine, and it is commercially available under the trademark LAMISIL™.

The '105 patent does not disclose a composition including one species from the group consisting of 2,2' –(alkyldioxy) bis-(alkyl-1,3,2-dioxyborinane) and 2,2'-oxybis(alkyl-1,3,2-dioxaborinane) as defined by claim 1 of the present invention. More generally, the '105 patent does not disclose a composition and method for the treatment of toenail fungus including an organo-boron compound. For these reasons, the composition and method for the topical treatment of toenail fungus recited by present claims 1 to 15 is submitted to be patentable over the '105 patent.

P. U.S. Patent No. 5,874,476 to Hsu et al.

U.S. Patent 5,874,476 to Hsu et al. (hereinafter the '476 patent) discloses a antimicrobial agent and a method of using the antimicrobial agent to inhibit the growth of microorganisms in, at, or on a locus subject to microbial attack. The antimicrobial agent described in the '476 patent are certain dihaloformaldoxime carbamates. The carbamates can be combined

with one or more other antimicrobial agents. Preferred known antimicrobial agents to be combined with the carbamates are methylenebis(thiocyanate); 5-chloro-2-methyl-4-isothiazolin-3-one; 2-methyl-4-isothiazolin-3-one; as 2-n-octyl-4-isothiazolin-3-one; 4,5-dichloro-2-n-octyl-4-isothiazolin-3-one; 1,2-benzisothiazolin-3-one; zinc 2-pyridinethiol-1-oxide; sodium 2-pyridinethiol-1-oxide; N'-›3,4-dichlorophenyl!-N,N-dimethylurea; 3-iodopropargyl-N-butylcarbamate; 10,10'-oxybisphenoxyarsine; 2-(thiocyanomethylthio)benzothiazole; 3-bromo-1-chloro-5,5-dimethylhydantoin; 2,2-dibromo-3-nitrilopropionamide; pentane-1,5-dial; and 2-bromo-2-nitro-1,3-propanediol.

The '476 patent does not disclose a composition including one species from the group consisting of 2,2' –(alkyldioxy) bis-(alkyl-1,3,2-dioxyborinane) and 2,2'-oxybis(alkyl-1,3,2-dioxaborinane) as defined by claim 1 of the present invention. More generally, the '476 patent does not disclose a composition and method for the treatment of toenail fungus including an organo-boron compound. For these reasons, the composition and method for the topical treatment of toenail fungus recited by present claims 1 to 15 is submitted to be patentable over the '476 patent.

Q. U.S. Patent No. 5,916,545 to Burnett et al.

U.S. Patent 5,916, 545 to Burnett et al. (hereinafter the '545 patent) discloses an antifungal nail solution. The antifungal solution comprises 1-{2,4-dichloro-.beta.-(2-chloro-3-thenyl)-oxy!phenethyl}imidazole (also known as ticonazole), water, alcohol, a water-soluble gel-forming agent and a plasticizer. The plasticizer is selected from the group consisting of propylene glycol isostearate, polysorbate, tocopheryl acetate, isopropyl acetate, myristate, and isopropyl palmitate. The hydrophilic gel-forming agent, which is used in the formulation of the present invention, may be any water-soluble resin derived from natural substances including cellulose, glucose, and sucrose. The preferred gel-forming agent is hydroxypropyl cellulose.

The '545 patent does not disclose a composition including one species from the group consisting of 2,2' –(alkyldioxy) bis-(alkyl-1,3,2-dioxyborinane) and 2,2'-oxybis(alkyl-1,3,2-dioxaborinane) as defined by claim 1 of the present invention. More generally, the '545 patent does not disclose a composition and method for the treatment of toenail fungus including an organo-boron compound. For the above reasons it is submitted that the applicants' claimed composition patentably defines over the '545 patent disclosure.

R. U.S. Patent No. 5,972,317 to Sorenson et al.

U.S. Patent 5,972,317 to Sorenson et al. (hereinafter the '317 patent) discloses a nail-permeable medication means for delivering a medicament through nails claws, hoofs or other similar hardened tissue of dermal derivation. The composition for treating the diseased nails and other dermal tissue comprises a proteolytic enzyme and a medicament. The medicament is selected for treatment of a particular disease condition. Examples of medicaments which may be used in the nail-permeable medication means include antibacterial, anti-viral, antifungal and other antimicrobial compositions. Such drugs may also be ionic, anionic, nonionic, cationic, zwitterionic, or ampholytic. Suitable drugs for use in the nail-permeable medication means include ciclopirox olamine, miconazole, tolnaftate, terbinafme, amorolfm and econazole.

The '317 patent does not disclose a composition including one species from the group consisting of 2,2' –(alkyldioxy) bis-(alkyl-1,3,2-dioxyborinane) and 2,2'-oxybis(alkyl-1,3,2-dioxaborinane) as defined by claim 1 of the present invention. More generally, the '317 patent does not disclose a composition and method for the treatment of toenail fungus including an organo-boron compound. For the above reasons, it is submitted that the applicants' claimed composition patentably defines over the '317 patent disclosure.

S. U.S. Patent No. 6,022,549 to Dyer

U.S. Patent 6,022,549 to Dyer (hereinafter the '549 patent) discloses an antimicrobial nail coating composition. The antimicrobial composition comprises an antimicrobial agent comprising a phenol, a film-forming polymer or resin and an organic solvent. In the preferred embodiment, the antimicrobial nail coating compositions include a benzalkonium chloride (BAC) compound. Suitable BAC homologs include N,N-dimethyldecyl ammonium chloride, N,N-dimethyl-undecyl ammonium chloride, N,N-dimethyldodecyl-ammonium chloride, N,N-dimethyltridecylammonium chloride, N,N-dimethyl-tetradecylammonium chloride, N,N-dimethylpentadecylammonium chloride, N,N-dimethylhexadecylammonium chloride, and N,N-dimethylhepta-decyl ammonium chloride. Other antimicrobial agents include quaternary amines and related compounds, cresols and resorcinols.

The '549 patent does not disclose a composition including one species from the group consisting of 2,2' –(alkyldioxy) bis-(alkyl-1,3,2-dioxyborinane) and 2,2'-oxybis(alkyl-1,3,2-dioxaborinane) as defined by claim 1 of the present invention. More generally, the '549 patent does not disclose a composition and method for the treatment of toenail fungus including an organo-boron compound. For these reasons, the composition and method for the topical treatment of toenail fungus recited by present claims 1 to 15 is submitted to be patentable over the '549 patent.

T. "Sax's Dangerous Properties of Industrial Materials", Tenth Edition, John Wiley & Sons, New York, P. 546 (2000)

Sax does not explicitly teach the compounds 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) nor 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane)of the subject topical application. Accordingly, Sax has no bearing on the novelty thereof. Significantly, the Sax disclosure provides strong evidence supporting the nonobviousness of using these compounds in a therapeutic application where safety and non-toxicity constitute critical criteria for utility. The "Safety Profile" of "Boron

Compounds" is reported by Sax to be "Very toxic"; so much so that "these Boron Compounds are said to be an industrial poison". The Sax teaching concerning toxicity of boron compounds points away from the topical application of the present invention. In doing so, it provides strong evidence that the composition and method for the topical treatment of toenail fungus defined by applicant's claims 1-15 are patentable.

U. Therapie, Paris, vol. 15, P. 791-802, (1960)

The Therapie reference describes the toxicity of the compound 2-(p-tolyl)-(5-methyl, 5-propyl)-1,3,2,-dioxiborinane (composition "I.S. 813") when used as a possible sedative. According to the reference, composition I.S. 813, when used as a sedative, exhibited very low toxicity. The composition I.S. 813 resembles the species of applicant's composition in that it contains a dioxiborinane moiety. However, it differs from the species of the applicant's claimed topical application in that (i) the I.S. 813 composition contains one rather than two dioxiborinane groups; and (ii) the substituents of the I.S. 813 composition are different. The Therapie reference has no bearing on the novelty of applicant's claimed topical application. Significantly, there is no suggestion in the reference that the composition might be useful for treating fungal infections. Although the Therapie reference contradicts the Sax teaching regarding toxicity of boron compounds, it falls far short of disclosing the compositional and procedural attributes of the composition and method for the topical treatment of toenail fungus recited by applicant's claims 1-15.

V. Material Safety Data Sheet BIOBOR JF®

This Material Safety Data Sheet lists the hazards of a fuel additive comprising, in combination: (i) 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-

dioxaborinane) nor 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) of the subject topical application; and (ii) 4.5% w/w of naptha. For the reasons set forth hereinabove in connection with the '548 patent, the topical application recited by applicant's claims 1-15 patentably defines over the Material Safety Data Sheet. Significantly, the Mateiral Safety Data Sheet provides strong evidence supporting patentability applicant's claims. Hazards listed by the reference include, "SKIN CONTACT: May cause slight to mild irritation". In addition, the Material Safety Data Sheet states: "Prolonged or repeated contact may dry the skin and lead to irritation (i.e. dermatitis)". These statements on the Material Safety Data Sheet point away from the invention defined by present claims 1-15, which contemplate use of a boron containing formulation as a topical treatment.

We note that the combined concentration of species 2,2' - (1-methyltrimethylene dioxy) bis - (4-methyl-1, 3, 2-dioxaborinane) nor 2,2' - oxybis (4, 4, 6 - trimethyl-1, 3, 2-dioxaborinane) in BIOBOR JF is 92.0%. This concentration may be significantly greater than that necessary and sufficient for an effective topical treatment. Dependent claims defining concentration limits considerably less than 92.0% would enhance the novelty of the present invention over the application of BIOBOR JF material taught by the Material Safety Data Sheet and provide an additional advantage, namely, less irritation potential.

Respectfully submitted,
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